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Role of Chest Computed Tomography in Prevention of Occupational Respiratory Disease: Review of Recent Literature

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Abstract

This review provides an update on literature published over the past 5 years that is relevant to using chest computed tomography (CT) as a tool for preventing occupational respiratory disease. An important area of investigation has been in the use of low-dose CT (LDCT) to screen asbestos-exposed populations for lung cancer. Two recent systematic reviews have reached conclusions in support of screening. Based on the limited evidence that is currently available, the Finnish Institute of Occupational Health has recommended LDCT screening in asbestos-exposed individuals if their personal combination of risk factors yields a risk for lung cancer equal to that needed for entry into the National Lung Screening Trial. It has also recommended further research, such as to document the optimal frequency of screening and the effectiveness of screening. Recent literature continues to support high-resolution CT (HRCT) as being more sensitive than chest radiography in detecting pneumoconiosis. However, there are insufficient data to determine the effectiveness of HRCT screening in improving individual outcomes if used in screening for pneumoconiosis and its routine use for this purpose cannot be recommended. However, if HRCT is used to evaluate populations, recent literature shows that the International Classification of HRCT for Occupational and Environmental Respiratory Diseases provides an important tool for reproducible evaluation and recording of findings. HRCT is an important tool for individual patient management and recent literature has documented that chest HRCT findings are significantly associated with outcomes such as pulmonary function and mortality.

Keywords

computed tomography; lung; pleura; occupational; work; surveillance; lung cancer; pneumoconiosis

Since the introduction of X-ray computed tomography (CT) into clinical medicine in the early 1970s, it has become an indispensable tool. CT allows far better visualization of anatomy than earlier technologies, improving clinicians' abilities to unambiguously

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Conflict of Interest

The author is a full-time employee of the U.S. Government and has no commercial conflicts to disclose. The findings and conclusions in this report are those of the author and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

recognize and diagnose disease processes, even at stages too mild to be recognized by conventional radiography. Importance of CT was quickly recognized, with Hounsfield and Cormack receiving the 1979 Nobel Prize in Medicine for their contributions to its development.¹ Because of great usefulness of CT, clinical usage has grown markedly in the United States, from approximately 3 million CT scans in 1980 to more than 62 million in 2006.²

In addition to its use in treating individual patients, there has been great interest in using chest CT as a tool for medical screening of populations. This is because CT offers the potential for early detection of diseases such as lung cancer where prognosis can be improved by early diagnosis and treatment.³⁻⁶ From the occupational standpoint, initial and periodic health evaluation of people put at risk for diseases by work-related exposures is often referred to as medical surveillance, medical monitoring, or medical screening. A direct impact of medical surveillance is “secondary prevention,” that is, identifying individuals at early stages of disease so that steps can be taken to prevent disease progression or provide more effective treatment. Medical surveillance can also motivate “primary prevention” if sentinel cases are recognized or if an excess burden of work-related disease is recognized and steps are taken to correct underlying problems such as hazardous work exposures, thereby protecting workers other than the affected individuals. Treatment of clinical work-related disease, which may occur if there is a failure of primary and secondary prevention, is called “tertiary prevention.”

The current review was undertaken to provide an update on recent literature relevant to using chest CT as a tool for preventing occupational respiratory disease. Major areas addressed include use of CT in screening of workers exposed to occupational carcinogens, such as asbestos, for early detection of lung cancer and use of CT in screening workers exposed to agents such as dusts to detect a range of nonmalignant pulmonary diseases. Literature addressing the significance of chest CT findings and comparing the relative performance of plain chest radiography and chest CT in detection of work-related pulmonary and pleural disease was also reviewed.

Sources of Literature Reviewed

To assure that literature from a broad range of sources was considered, an inclusive PubMed search using the terms “computed tomography” and “lung” or “pleura” AND “occupational” was performed on September 10, 2014. The search identified 269 articles entered into PubMed from January, 2009 through the search date. Titles and abstracts were reviewed and 65 English-language articles were selected as relevant to the focus of the review. There were 47 original investigations touching on use of chest CT for work-related conditions (Table 1). In general, case reports were not selected, but 2 of the 47 were included because they demonstrated novel and potentially useful high-resolution CT (HRCT) patterns after exposure to coal mine dust⁷ and tungsten/hard metal.⁸ There were 17 reviews and 1 proceeding report (Table 2). One of these was a systematic review and meta-analysis describing associations between chest CT findings and pulmonary function in asbestos-exposed workers.⁹ This initial list of articles was supplemented with others identified from the reference lists of the articles or known to the author. These are cited in the text. Two key

references added in this fashion were a structured review¹⁰ and a structured review with a meta-analysis¹¹ of screening asbestos-exposed individuals for lung cancer with low-dose CT (LDCT).

Overview of Computed Tomography Technology

CT technology has evolved greatly in recent years.¹ The basic technology involves irradiating the patient with X-rays and detecting transmission on the opposite side of the body at multiple angles (usually a complete 360 degrees) around the part being imaged. Mathematical algorithms allow computation of X-ray attenuation within small volume units of the body part, allowing reconstruction and visualization of its internal structure. Since the late 1990s, CT scanners have become available with increasing numbers of detector channels or arrays. These multiple-detector-row scanners can image larger volume slices with each rotation of the CT gantry, allowing scans to be completed in shorter periods of time. CT scanners use two basic scanning modes. Axial (sequential) scanning involves intermittent movement of the patient relative to the tube and detector array resulting in collection of data from sequential volume slices. Helical (spiral) scanning involves continuous movement of the patient with continuous rotation of the tube and detector array. The resulting continuous “spiral” data allows for reconstruction of overlapping image slices. It also decreases overall scanning time. Either technology can be used to reconstruct HRCT images, that is, images with narrow slice widths (approximately 1–2 mm) and high spatial resolution.

The chest CT procedure, which involves reconstructing images from multiple radiation exposures, delivers more radiation to patients than plain chest radiography. The radiation dose associated with performing a posteroanterior chest radiograph is 0.05 mSv.¹² Median exposure associated with performing a routine chest CT without contrast was recently reported as 8 mSv.¹³ Chest CTs can be performed using less radiation, although this can involve technical compromises affecting spatial resolution and image quality. The LDCT protocol used in the National Lung Screening Trial (NLST) randomized controlled trial of LDCT screening for lung cancer in high-risk current and former smokers achieved acceptable visualization of nodules and reduced the average effective radiation dose to 1.5 mSv.¹⁴

General Considerations for Medical Screening with Chest Computed Tomography

General considerations for medical surveillance in other settings and with other tests also apply to medical screening with chest CT.¹⁵ Ability to maximize the desired benefits and minimize the undesired harms of screening is related to test performance in identifying the disease of interest. Statistical terms used to describe test performance include sensitivity (the probability that the test is positive in individuals with the disease), specificity (the probability that the test is negative in individuals who do not have the disease), positive predictive value (PPV; the probability that an individual with a positive test has the disease) and negative predictive value (NPV; the probability that an individual with a negative test does not have the disease). PPV and NPV can be greatly affected by the prevalence of the

targeted disease in the screened population. For example, if there is a low prevalence, false positive results associated with imperfect sensitivity may greatly outnumber true positive results, resulting in a low PPV. In this situation, many of the follow-up medical evaluations triggered by screening might not confirm the presence of disease, adversely affecting the cost-benefit of screening. Thus, a useful strategy for improving the cost-benefit of medical surveillance is to target screening to populations at high risk for the disease of interest.

Another important reason to target screening to populations with the greatest potential for benefit is to assure that the screening benefits outweigh the undesired harm of cancer from radiation used to perform CTs. Although this risk is relatively small, it is a real consideration at the population level. It has been estimated that one radiation-induced cancer would result from 1,090 routine chest CTs without contrast with 8 mSv radiation dose in 60 year old women or 2,080 such studies in 60 year old men.¹³ Lifetime risk is related to factors including gender, age, and radiation dose. Thus, risk can be lowered by increasing the age at which studies are done and by reducing cumulative radiation dose. Another factor affecting lifetime risk is smoking, with synergism between cumulative radiation exposure and smoking in causing lung cancer.¹⁶

If medical screening is undertaken, it must be conducted appropriately. At the individual level, workers must receive timely notification of their results and be provided with appropriate counseling and appropriate follow-up medical care. Also, surveillance must be conducted in a fashion that protects individual confidentiality and is consistent with ethical and legal requirements for confidentiality. If surveillance identifies sentinel cases or disease clusters suggesting a wider problem and a need for improved primary prevention, this information should be acted upon and in a way that protects individual confidentiality. In addition, when appropriate, arrangements should be made for evaluation of aggregate results at the population level to assess for unrecognized associations between work and risk for disease, providing new opportunities for primary prevention. Again, this must be done in a way that protects individual confidentiality.

Screening for Occupationally Related Lung Cancer with Low-Dose Computed Tomography

The initial publication of findings from the NLST in 2011 documenting the effectiveness of LDCT screening in current and former heavy smokers and its superiority to screening with chest radiography,³ and the subsequent publication by the U.S. Preventative Services Task Force (USPSTF) of recommendations for use of LDCT in screening for lung cancer¹⁷ were important public health landmarks. USPSTF summarized its recommendations as follows:

“The USPSTF recommends annual screening for lung cancer with LDCT in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.”¹⁷

The USPSTF carefully balanced benefits of screening against potential harms in making its recommendation. It estimated that its recommended approach to screening would reduce

lung cancer mortality by 14%, with an absolute reduction of 521 lung cancer deaths per 100,000 persons in the population. The most important harm it identified was “overdiagnosis” of lung cancers that would not have been identified during a person’s life without screening. Rate of overdiagnosis was estimated to be 10% of screen-detected cases. Lifetime incidence of radiation-induced lung cancer deaths was estimated to be less than 1%. USPSTF emphasized the importance of considering functional status and the presence of other comorbid conditions in making decisions about screening. It emphasized the importance of shared decision-making with those being screened. USPSTF also emphasized the importance of appropriate follow-up evaluation of LDCT findings, using an organized approach such as that detailed in National Comprehensive Cancer Network (NCCN) guidelines.¹⁸

In its recommendation, USPSTF acknowledged that “in addition to age and smoking history, such risk factors as occupational exposure, family history, and history of other lung diseases are important when assessing patients’ risks for lung cancer.” However, these other risk factors do not factor into the current USPSTF screening recommendations.

Although most professional organizations’ recommendations for LDCT screening for lung cancer in high-risk populations parallel those of the USPSTF, two have issued recommendations that take occupational risk factors into account. NCCN recommends that those who meet screening criteria similar to those established by the USPSTF be screened. However, it also recommends LDCT screening for people aged 50 and older with smoking histories of 20 or greater pack-years and one additional risk factor other than second-hand smoke. These other risk factors include radon exposure, occupational exposure, history of certain cancers, chronic obstructive pulmonary disease, pulmonary fibrosis, and family history of lung cancer. Specific occupational exposures mentioned in the guideline include arsenic, chromium, asbestos, nickel, cadmium, beryllium, silica, diesel fumes, coal smoke, and soot. The NCCN guidelines do not specify a threshold for level of exposure to an occupational agent that is necessary to trigger surveillance.¹⁸

The American Association for Thoracic Surgery issued guidelines in 2012 that recommend the following:

“...annual lung cancer screening with low-dose computed tomography screening for North Americans from age 55 to 79 years with a 30 pack-year history of smoking. Long-term lung cancer survivors should have annual low-dose computed tomography to detect second primary lung cancer until the age of 79 years. Annual low-dose computed tomography lung cancer screening should be offered starting at age 50 years with a 20 pack-year history if there is an additional cumulative risk of developing lung cancer of 5% or greater over the following 5 years....”¹⁹

The recommendations note that occupational and environmental exposures should be considered in establishing whether the threshold of risk for developing lung cancer over the next 5 years is reached.

Two systematic reviews have assessed the potential impact of LDCT screening for lung cancer in asbestos-exposed workers.^{10,11} Ollier et al conducted a systematic review and

meta-analysis.¹¹ They identified seven relevant cohort studies. Documentation of level of asbestos exposure varied between studies. Five of the studies reported asbestos exposure duration, which ranged from 17.7 to 30 years. Two of the studies did not report exposure duration. Only one study reported time since first exposure. Median or mean ages of participants reported by the studies ranged between 58 and 68 years. The main finding of the meta-analysis of data representing approximately 5,000 workers was that lung cancer was detected by LDCT scan with a prevalence of 1.1% (95% confidence interval, 0.6–1.8%). The proportion of stage I cancers, the most treatable group, ranged in the studies from 20 to 100%. The authors concluded that this prevalence of lung cancer and frequency of stage I screening diagnoses were similar to those reported by the NLST in screening heavy smokers.³ Therefore, “screening asbestos-exposed workers could reduce mortality in proportions previously observed among heavy smokers and, thus, should not be neglected, particularly for individuals combining both exposures.”¹¹ The authors noted that further investigation was needed to identify the subset of asbestos-exposed workers who would benefit most from screening and that a large, randomized controlled trial was urgently needed to identify the best frequency of screening for both heavy smokers and asbestos-exposed workers.

Another systematic review of LDCT screening of asbestos-exposed workers for lung cancer was sponsored by the Finnish Institute of Occupational Health (FIOH).¹⁰ Vehmas et al “searched for original studies on screening for lung cancer in asbestos-exposed workers.” A total of 12 articles were identified. The review noted that the studies were heterogeneous in methodology and were “...case series with a limited number of subjects, no control groups, and little follow-up data on mortality, providing only weak if any inferential evidence about the efficacy of lung cancer screening specifically targeted to adults with a history of asbestos exposure.” However, similar to Ollier et al, Vehmas et al note that “...the available evidence indicates that LDCT screening in this population detects asymptomatic lung cancer at a favorable stage similar to the performance that has been observed in high risk former and current smokers.”

Despite the limitations of the available literature, Vehmas et al concluded that it was reasonable to offer LDCT screening to certain asbestos-exposed individuals. A summary report prepared by FIOH recommends LDCT screening of workers “... with any asbestos exposure and a smoking history equal to the entry criteria of the NLST study; and workers with asbestos exposure, with or without a smoking history, which alone or together would yield an estimated risk level of lung cancer equal to that in the entry criteria of the NLST study.”²⁰ The estimated absolute risk threshold is 1.34% over 6 years.¹⁰ FIOH also calls for additional research to address factors such as improving ability to assess lung cancer risk, assess the optimal frequency of screening (annual vs. biennial) and document effectiveness.

Eight recent original articles touching on lung cancer screening were identified by the current literature search (Table 1). Of note were two articles addressing psychological distress potentially associated with screening. One noted that, at baseline, psychological stress is higher in asbestos-exposed individuals than controls and is associated with self-perception of intensity of exposure and resulting risk of future disease.²¹ Another found that anxiety decreased after LDCT lung cancer screening and did not differ between those who

received clear results and those who required follow-up.²² Another provided an updated estimate of radiation risk associated with lung cancer screening under current recommendations, emphasizing the importance of taking cumulative exposures into consideration.²³ An additional article identified by the search evaluated the prognostic significance of calcifications of arteries in the chest, an incidental finding in LDCT screening for lung cancer. It found an association between calcifications of the left anterior descending coronary artery and calcifications of the brachiocephalic origin with cardiovascular death.²⁴

Screening for Pneumoconiosis with High-Resolution Computed Tomography

Screening dust-exposed workers with chest radiography to identify cases of pneumoconiosis is a well-established practice throughout the world.^{25,26} In general, surveillance is conducted at a periodicity of about every 3 to 5 years and the International Labor Organization (ILO) classification system is used to “classify” plain chest images for the presence and severity of pulmonary and pleural changes associated with pneumoconiosis.²⁷ This helps to assure that results of screening are reproducibly recorded across regions and across time. It is well-established in the literature that chest HRCT has greater sensitivity for detecting pneumoconiosis and individual features of pneumoconiosis, such as progressive massive fibrosis, in workers exposed to asbestos, silica, and coal dust.^{25,28,29} Thus, there has been interest in use of HRCT for screening. However, pneumoconiosis differs somewhat from lung cancer in that there is not a similar wealth of data to show that detection at an early stage provided by a screening program has a beneficial impact on outcome or that the earlier detection potentially provided by HRCT over chest radiography would be sufficiently beneficial to support use of HRCT. A recent review of asbestos-related surveillance sponsored by FIOH noted that there “...was little specific scientific evidence of the health benefits of such surveillance.”²⁰

Despite limitations of the evidence, the review noted that there were potential benefits to early detection of nonmalignant diseases (such as pneumoconiosis) including the opportunity to reduce exposures, to create an incentive to cease smoking, to encourage other measures such as vaccinations to reduce respiratory infections, and to use screening as an opportunity to increase the health knowledge of screening participants.^{20,25} At the population level, analysis of aggregated chest radiography screening data can identify problems that might otherwise go unrecognized and motivate action to improve primary prevention. The U.S. experience with coal workers’ pneumoconiosis is an example of this.^{30,31}

HRCT is clearly useful for clinical care (tertiary prevention) of pneumoconiosis. FIOH noted that CT may be particularly useful when there is a borderline finding of lung fibrosis by chest radiography; there is a discrepancy between lung function and radiographic findings; or widespread pleural changes severely hamper the ability to visualize lung parenchyma with chest radiography.²⁰

In cases where HRCT screening for pneumoconiosis is contemplated (e.g., in an epidemiological investigation) it is important to have a standardized approach for recording the presence and severity of pulmonary and pleural changes. This helps to assure reproducibility of results between readers, across regions, and over time, which is very important for research, surveillance, legal, and compensation purposes. Thus, a classification system similar to the ILO system has been developed for HRCTs, called the International Classification of HRCT for Occupational and Environmental Diseases (ICOERD).^{32,33} Findings classified include well-defined rounded opacities, irregular and/or linear opacities, inhomogeneous attenuation, ground glass opacity, honeycombing, emphysema, large opacities, pleural abnormalities, and pleural calcifications. Over the past decade, the ICOERD system has achieved much international acceptance.²⁰

Six articles identified by the literature review involved use of the ICOERD system. Each is briefly described in Table 1. Of particular note is a reading trial involving 7 independent readers evaluating images from 27 pneumoconiosis patients and 7 normal individuals in 2 separate reading trials. There was moderate-to-good agreement between the readers for all areas of the classification except ground glass opacities. Overall agreement was felt to be sufficient to support use of the system.³³ Another article documenting interreader agreement reported similar results.³⁴ An addition to the ICOERD system was published in 2012 for reading CT images of malignant pleural mesothelioma.³⁵

Additional Issues Addressed by Recent Articles

Asbestos

Fifteen original articles identified by the literature search addressed asbestos-related issues (Table 1). Two articles add to the previous observations that HRCT is more sensitive than chest radiography in identifying asbestos-related changes.^{36,37} One article documents the superiority of CT in identifying pleural plaques in obese individuals in the United States,³⁸ although a study in Japan found that chest radiographs were an acceptable screening tool for pleural plaques in that country.³⁹

Several studies evaluated health implications of HRCT findings. One study noted an association between the presence of parietal and/or diaphragmatic pleural plaques and small, but statistically significant, decreases in total lung capacity (TLC), forced vital capacity (FVC), and forced expiratory volume in 1 second (FEV₁). Also, a significant relationship was found between extent of plaques and reduction in TLC and FEV₁.⁴⁰ Another found a relationship between pleural plaque and risk for incident mesothelioma.⁴¹ Pulmonary parenchymal findings on HRCT were associated with reduced lung function,^{42–44} pulmonary inflammation,⁴⁵ all-cause mortality⁴⁶ (extent of pleural plaque was also associated), and pneumonia mortality.⁴⁷ A systematic review and meta-analysis documented relationships between asbestos-related radiographic findings and lung function changes. Reduction in lung function was greater if radiographic findings were based on chest radiography than if they were based on CT, perhaps because of the ability of CT to detect more minimal disease.⁹

Silica

Three articles focused on silica-related issues (Table 1).^{48–50} An additional article using the ICOERD system assessed primarily silica-exposed workers.³⁴ Recent articles continue to support better sensitivity of HRCT than chest radiography in detecting silica-associated lung disease.^{34,48} One article suggests that counts of micronodules < 3 mm might be useful for detecting early stages of silicosis.⁴⁹

Other Conditions

Two articles address HRCT findings in workers exposed to indium compounds.^{51,52} They show that exposure to these compounds can be associated with HRCT findings of pulmonary alveolar proteinosis, pulmonary fibrosis, and emphysema and suggest that there may be a progression from alveolar proteinosis to the other conditions. An article evaluating welders found that HRCT was far more sensitive in detecting welder lung disease than chest radiography.⁵³ Case reports of potentially novel findings in response to exposures documented diffuse ground glass opacities resembling hypersensitivity pneumonitis after exposure to hard metal⁸ and diffuse interlobar septal thickening after exposure to coal mine dust.⁷ Other articles described CT findings after exposure to World Trade Center dust,⁵⁴ in Turkish coppersmiths,⁵⁵ in diesel-exposed toll collectors,⁵⁶ and in workers exposed to polyvinyl chloride dust.⁵⁷ One article notes the usefulness of 18-fluorine-labeled 2-deoxy-2-fluoro-D-glucose positron emission tomography/CT (FDG-PET/CT) in evaluating local extent, lymph node involvement, and metastasis of epithelial malignant mesothelioma.⁵⁸ Another notes preexisting literature indicating false-positive PET scans in the presence of pneumoconiosis, but presents four cases where FDG-PET/CT was able to differentiate between cancer and pneumoconiosis and was useful in patient management.⁵⁹ One article evaluating flight attendants noted an association between the extent of second-hand tobacco smoke exposure and the extent of coronary artery calcification.⁶⁰ A review notes the imperfect sensitivity of HRCT in detecting obliterative bronchiolitis (Table 2).⁶¹ It cites a report evaluating returning veterans of Afghanistan and Iraq, where 25 of 37 HRCTs in biopsy-proven cases were normal and only 6 showed evidence of air trapping.⁶² This finding occurred despite the HRCTs having been performed on inspiration and expiration, and despite efforts to identify features of the condition, such as centrilobular nodularity and expiratory air trapping.^{62,63}

Summary

The ability to visualize thoracic anatomy with chest CT has made it a well-established and indispensable clinical tool. Similarly, chest CT plays an important and evolving role in preventing occupational respiratory disease. General considerations in using chest CT to screen occupationally exposed populations are similar to those for other medical screening tests. Test performance in identifying the disease of interest, identifying high-risk populations most likely to benefit from screening, performing screening in an ethical fashion that protects confidentiality, and assuring that screening results are appropriately reported and acted upon at the individual and population levels are all important considerations. Two recent systematic reviews have reached conclusions in support of screening asbestos-exposed populations for lung cancer with LDCT. Based on the limited evidence that is

available, FIOH has recommended such screening in asbestos-exposed individuals if their personal combination of risk factors yields a risk for lung cancer equal to that needed for entry into the NLST. However, FIOH and others have also called for further research, such as to document the optimal frequency of screening and the effectiveness of screening. Although, HRCT is more sensitive than chest radiography in detecting pneumoconiosis, there are insufficient data to determine the effectiveness of HRCT screening in improving individual outcomes if used in screening for pneumoconiosis and it cannot be recommended at this time. However, if HRCT is used to evaluate populations, recent literature shows that the ICOERD classification system provides an important tool for reproducible evaluation and recording of findings. HRCT is very useful in individual patient management and recent literature has documented that chest HRCT findings are significantly associated with outcomes such as pulmonary function and mortality.

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Table 1

Original investigations identified by literature search

Subject area/reference	Type of study	Comment
Lung cancer screening with LDCT		
Clin et al (2009) ⁶⁴	Observational, no control (cohort)	Compared performance of biennial plain chest image and monodetector chest CT scan in screening 972 individuals who had been highly exposed to asbestos. Twenty-four lung cancers occurred over a follow-up period of 2 years. CT scan detected 20 cancers, 12 of which had not been detected by chest radiograph. Based on receiver operating characteristic curve analysis, recommended 5 mm diameter as a threshold value for considering noncalcified nodules as "suspect"
Clin et al (2011) ⁶⁵	Observational, no control (cohort)	Evaluated 5,662 asbestos-exposed retirees with spiral CT. Excess incidence of primary lung cancer (SIR = 1.95) and pleural mesothelioma (SIR = 11.88) observed among those presenting with nodules. No relationship between pulmonary nodules and asbestos exposure or presence of nonmalignant asbestos-related disease
Felten et al (2014) ⁶⁶	Observational, no control (cohort)	Formerly asbestos-exposed power industry workers ($n = 187$) underwent low-dose spiral CT and sputum cytology at least once with follow-up for at least 3 years. Twelve lung cancers occurred. Sensitivity/specificity of sputum cytology = 58%/98%; of LDCT 92%/97%
Maurel et al (2009) ²¹	Observational, with control (cross-sectional)	Evaluated psychological distress at baseline in 3,122 asbestos-exposed subjects and 486 controls. Distress was higher in asbestos-exposed and related to self-perception of intensity of exposure and risk of current or future disease from exposure
McCunney and Li (2014) ²³	Mathematical modeling	Estimated radiation exposures for LDCT screening based on NLST. Estimated 2 mSv dose for LDCT and 8 mSv for diagnostic scans used to follow-up nodules. Suggest that current lung cancer screening protocols, if conducted over 20- to 30-year periods, can increase the risk of lung cancer beyond cigarette smoking as a result of cumulative radiation exposure
Roberts et al (2009) ⁶⁷	Observational, no control (cohort)	LDCT used to screen prior asbestos workers (507 men, 9 women, median age 60 y). Annual repeat performed in 356 workers. Pulmonary nodules found in 371, at least 5 mm in 91. Identified 6 lung cancer and 4 mesothelioma cases (2 pleura, 2 peritoneal) at baseline or annual scans. An additional 1 lung cancer and 3 mesotheliomas presented at times other than screening. Three screen-detected lung cancers were stage 1 and remained alive. Two were not staged, 2 were lost to follow-up. All mesothelioma patients died soon after diagnosis
Sancini et al (2010) ⁶⁸	Observational, with control (cross-sectional)	Evaluated 100 Italian urban traffic policeman and 100 controls not exposed to urban pollutants with low-dose spiral CT. Showed an interaction between urban pollutant exposure and smoking, which greatly increased the risk of finding suspicious lung nodules with diameters between 5 and 10 mm
Vierikko et al (2009) ²²	Observational, no control (cohort)	Asbestos-exposed workers screened with chest CT ($n = 633$). Health anxiety was reduced significantly after screening ($p < 0.001$). After 1 y, no significant long-term psychological differences were found between those who immediately received clear results and those who were submitted to additional examinations because of positive findings
ICOERD^a		
Berk et al (2014) ⁶⁹	Observational, no control (cross-sectional)	Evaluated 32 Turkish dental technicians, mean age 31 y, mean employment duration 14 y. Compared CXR classified using ILO ^b system with HRCT classified using ICOERD. Parenchymal opacities identified in 22 by HRCT and 10 by CXR. Positive correlations between ICOERD and ILO scores
Bhawna et al (2013) ⁷⁰	Observational, no control (cross-sectional)	Retrospective review of 119 industrial workers seen in an Indian medical center and evaluated with chest X-ray and HRCT, which was evaluated using the ICOERD system. Notes that chest radiography was normal in 53 patients, but that 46 of them had positive findings on HRCT
Meijer et al (2011) ³⁴	Observational, no control (cross-sectional)	Construction workers ($n = 79$), mean age 49.6, mean tenure in construction 21 y, were evaluated by chest X-ray with ILO classification by at least 2 readers and HRCT with ICOERD classification by 3 readers. In the 63 workers with ILO profusion 0/0, HRCT showed that 8% had round opacities, 22% irregular/linear opacities, 41% emphysema, and 6% ground glass. HRCT well-defined round opacities, consistent with nodular silicosis, were associated with

Subject area/reference	Type of study	Comment
		cumulative quartz exposure. Kappa tests for agreement between readers. Presence of rounded opacities: HRCT -0.69, CXR -0.68. Pleural changes: HRCT -0.61, pleural changes -0.79. Irregular opacities: HRCT -0.23, CXR -0.14. Additional kappa values for HRCT: pleural calcification -0.74, emphysema -0.59
Suganuma et al (2009) ³³	Observational, no control (reading trial)	Evaluation of ICOERD performance in reproducibly recording the presence and severity of HRCT changes associated with occupational and environmental respiratory disease. Seven independent readers evaluated images from 27 pneumoconiosis patients and 7 normal individuals in 2 separate reading trials. Agreement was moderate- to-good for rounded opacities (weighted kappa = 0.68 and 0.64), irregular opacities (0.59, 0.48), honeycombing (0.65, 0.47), emphysema (0.76, 0.62), and large opacities (0.48, 0.52). Ground glass opacities (0.16, 0.20) showed poor-to-fair agreement
Vehmas and Oksa (2014) ⁷¹	Observational, no control (cohort)	Asbestos-exposed workers ($n = 633$) evaluated with ICOERD system and findings assessed as risk factors for mortality in the subsequent 119 deaths, mostly from neoplasms and benign respiratory disease. Irregular/linear opacities, honeycombing, emphysema, large opacities, visceral pleural abnormalities, and bronchial wall thickening were all significantly related to all-cause deaths. Emphysema and visceral pleural abnormalities predicted deaths from cardiovascular disease
Zhou et al (2012) ³⁵	Guideline development based on systematic literature review and expert opinion	Publication describes development and validation of a guideline on reading CT images of malignant pleural mesothelioma based on 10 features described in the literature as frequently observed in cases: unilateral pleural effusion (ue), nodular pleural thickening (nt), interlobar fissure thickening (it), mediastinal pleural thickening (mt), tumoral encasement of lung (te), calcified plaque engulfment (pe), invasion (iv), diminished lung (dl), contracted hemithorax (ch) and pleural mass (pm). The guideline is a supplement to ICOERD
Asbestos		
Comparison of CT and chest radiography		
Elshazley et al (2011) ³⁹	Observational, no control (cross-sectional)	Evaluated chest images of 140 Japanese asbestos-exposed construction workers by CXR and chest CT. Images seen on CXR were confirmed with high frequency by CT, except "tapered laterally (short type)." Concluded that CXR remained a suitable tool for screening asbestos-related pleural plaques due to simplicity, low radiation exposure, wide availability, and cost-effectiveness
Larson et al, 2014 ³⁸	Observational, no control (cross-sectional)	Patients being screened for asbestos-related health outcomes had digital chest image and chest HRCT ($n = 200$). Chest images were evaluated using the ILO system by 7 B Readers. Chest HRCT images evaluated by 2 thoracic radiologists were used as a gold standard. False-positive radiograph evaluations increased with increasing BMI. It was concluded that clinicians should be cautious in evaluating radiographs of younger obese persons for asbestos-related pleural plaques, especially in populations anticipated to have a low prevalence
Ochsmann et al (2010) ⁷²	Observational, no control (reading trial)	Observer pairs ($n = 10$) classified CXRs (using the ILO classification system) and chest CT scans (using a customized classification system) of 635 formerly asbestos-exposed workers. Interobserver variability assessed as kappa values were similar for CXRs and CT scans. It was hypothesized that this might be due to the selected nature of the population, with discrete radiographic changes; and to unfamiliarity with the CT classification system
Ryan et al (2011) ³⁶	Observational, no control (cross-sectional)	Study evaluated 34 participants with exposure to erionite from work in contaminated gravel pits, road work with contaminated gravel, or both. HRCT-identified interstitial changes in 6; chest radiograph only in 1. HRCT-identified pleural changes in 3; chest radiograph only in 1
Spyratos et al (2012) ³⁷	Observational, no control (cross-sectional)	Studied 266 asbestos cement factory employees. Sensitivity of CXR was 43% compared with HRCT as the gold standard. Authors concluded that HRCT was much more sensitive. After adjustments for age, smoking, and years of occupational exposure, lung function impairment (TLC and DLCO) was related to parenchymal and visceral pleural HRCT abnormalities, but not to parietal pleural HRCT abnormalities.
Health implications of CT findings in asbestos-exposed individuals		

Subject area/reference	Type of study	Comment
Clin et al (2011) ⁴⁰	Observational, no control (cross-sectional)	Evaluated 2,743 subjects with previous asbestos exposure. A relationship was found between presence of parietal and/or diaphragmatic pleural plaques and small, but statistically significant, decreases in TLC, FVC, and FEV ₁ . A significant relationship was found between extent of pleural plaques and reduction in TLC and FVC
Kishimoto et al (2011) ⁷³	Observational, no control (case series)	Evaluated ability of HRCT to differentiate between chronic interstitial pneumonias and asbestosis. Evaluated 38 cases with clinical diagnosis asbestosis. Total 17 felt to have asbestosis by histopathology; 13 by HRCT, and 10 by both
Lehtimäki et al (2010) ⁴⁵	Observational, no control (cross-sectional)	Evaluated 104 subjects with moderate-to-high occupational asbestos exposure. After excluding other lung diseases, 35 had normal parenchymal findings on HRCT and 31 borderline findings. Those with borderline findings had increased levels of exhaled NO and increased inflammatory markers in breath condensate
Mastrangelo et al (2009) ⁷⁴	Observational, no control (cross-sectional)	Evaluated 772 formerly exposed asbestos workers. Used LDCT ("X-ray dose ranged from 20 to 40 mAs; 7 to 8 mm thick lung scans were systematically reconstructed") to identify asbestos-related diseases and assessed dose-response relationships. Significant relationships: asbestosis—cumulative exposure; pleural plaques—time since first exposure and peak exposure; diffuse pleural thickening—time since first exposure
Nogueira et al (2011) ⁴²	Observational, no control (cohort)	Followed 63 exposed workers with mild-to-moderate asbestosis for 3–9 y. Workers whose interstitial markings on HRCT progressed had greater decline in CO diffusing capacity. Progression of HRCT abnormalities was best reflected by CO diffusing capacity and not reflected by spirometry
Pairon et al (2013) ⁴¹	Observational, no control (cohort)	Follow-up study of 5,287 male subjects with previous occupational exposure to asbestos. Followed for 7 y. Pleural plaque identified by CT was a risk factor for incident pleural mesothelioma (unadjusted HR = 8.9, 95% CI = 3.0–26.5; adjusted HR = 6.8, 95% CI = 2.2–21.4 after adjustment for time since first exposure and cumulative exposure index to asbestos)
Piirila et al (2009) ⁴³	Observational, no control (cohort)	Evaluated 590 asbestos-exposed workers, 95% of whom were smokers or exsmokers. "FVC and TLC were negatively correlated with fibrosis score, parenchymal bands, extent of pleural thickenings, and positively with widened retrosternal space. FEV ₁ /FVC ratio was negatively correlated with emphysema types and widened retrosternal space and positively with parenchymal bands and subpleural nodules. Thickened bronchial walls did not separate between restrictive and obstructive ventilatory function"
Vehmas et al (2012) ⁴⁶	Observational, no control (cohort)	Construction workers (<i>n</i> = 584) followed for a mean of 10.5 y. Total 185 deaths occurred. CT signs of emphysema, pulmonary fibrosis, ground glass opacities, thickened bronchial walls, pleural plaque extent, and adhesions were significant predictors of all-cause death
Vehmas et al (2012) ⁴⁷	Observational, no control (cohort)	Asbestos-exposed construction workers (<i>n</i> = 590) underwent LDCT for lung cancer screening and followed a mean of 10.44 y. "Definite interstitial fibrosis" on CT scan associated with increased pneumonia mortality (HR 3.7, 95% CI 1.22–11.23). "Some interstitial fibrosis" on CT associated with borderline statistically significant increase (HR 2.26, 95% CI 0.98–5.19)
Vierikko et al (2010) ⁴⁴	Observational, no control (cross-sectional)	Evaluated asbestos-exposed workers who participated in a CT lung cancer screening program. Overall, 86 had pulmonary fibrosis and 541 did not. In multivariate analyses, age, FEV ₁ /FVC ratio, and poor diffusing capacity were associated with HRCT fibrosis
Silica		
Athavale et al (2011) ⁴⁸	Observational, no control (cross-sectional)	Indian flour mill workers (<i>n</i> = 56, mean age 42 y) evaluated by CXR evaluated by a single reader and HRCT (evaluation method not specified). Exposed to silica by grinding grain between silica-containing stones (~80% silica content) and steel wheels. Thirty-four of 56 had abnormal CXR findings. Two had PMF. CT was not done in 2 due to active TB. Total 44/54 of the remainder had abnormal HRCT. Overall, 50% calcified lymph nodes, 46% parenchymal nodules, 44% fibrotic scarring, 43% bronchiectasis, 22% pleural thickening, and 20% emphysema/air trapping
Mets et al (2012) ⁴⁹	Observational, with control (cross-sectional)	Evaluated 54 male smokers with severe silica dust exposure and 54 male control smokers (participating in a study of lung cancer screening) with low-dose chest CT. Evaluated counts of solid micronodules < 3 mm. Upper 95th confidence limit in the controls was 13 micronodules. Twelve of the dust-exposed subjects had counts greater than that upper limit. Micronodules were

Subject area/reference	Type of study	Comment
		found with significantly greater frequency in upper than in middle or lower lobes. The authors concluded that increased micronodule counts on chest CT scan might represent an early stage of silicosis
Ozmen et al (2010) ⁵⁰	Observational, no control (cross-sectional)	Sixty consecutive men with a history of exposure to silica during denim sandblasting were evaluated using a 64-row multidetector CT. Silicosis was found by imaging in 44. Nodules were present in all cases with centrilobular type in 64%. Nodules were most often seen in all lung zones. Nodular profusion score was significantly correlated with duration of silica exposure, latency period, presence of progressive massive fibrosis, and pleural thickening. Enlarged lymphadenopathy was observed in 45.5% of the patients
Other occupational respiratory diseases		
Caplan-Shaw et al (2011) ⁵⁴	Observational, no control (case series)	Twelve symptomatic WTC-exposed patients underwent HRCT and lung biopsy. Six had predominant interstitial (reticular) densities and 6 had abnormal lung function tests and HRCT findings of "airway" disease defined as diffuse bronchial wall thickening, air trapping, or other abnormalities of the airways in the absence of interstitial findings. In the interstitial group, HRCT findings of reticulation, traction bronchiectasis, honeycombing, bronchial wall thickening or dilation, and mosaic attenuation or air trapping occurred in at least 3 of the 6 patients
Cummings et al (2012) ⁵²	Observational, no control (case series)	International meeting evaluated 10 men who produced used or reclaimed indium compounds. Interstitial lung disease was diagnosed in 7 at 4 to 13 y after exposure and pulmonary alveolar proteinosis in 3 at 1 to 2 y after first exposure. Two of the ILD cases had pneumothoraces. It was concluded that the evidence suggested that indium compounds cause a novel lung disease that may begin with pulmonary alveolar proteinosis and progress to fibrosis, emphysema, and in some cases premature death
Cummings et al (2010) ⁵¹	Observational, no control (case series)	Describes 2 cases of pulmonary alveolar proteinosis in workers at a facility producing indium tin oxide
Dagli et al (2010) ⁵⁵	Observational, no control (cross-sectional)	Evaluated 30 Turkish coppersmiths, mean age 48 y. Seventeen had abnormal HRCT findings, with centrilobular micronodules being the most prevalent finding, with ground glass, paraseptal emphysema, and subpleural cysts also occurring at relatively high frequencies
Okuno et al (2010) ⁸	Observational, no control (case report)	Case report of a 42-year-old mine who had worked as a metal grinder for 3 y. He presented with exertional dyspnea and pathological evaluation of lung tissue suggested hard metal pneumoconiosis associated with tungsten. HRCT showed diffuse ground glass opacities resembling findings of hypersensitivity pneumonitis
Safak et al (2010) ⁵⁶	Observational, no control (cross-sectional)	Diesel-exposed toll collectors evaluated by CXR ($n = 120$). Helical CT performed in 40 whose plain chest radiographs showed hyperinflation and linear markings. Several findings reported: "A positive correlation was observed between age and the right upper bronchus wall thickness ($r = 0.577$, $p = 0.000$). An inverse correlation was found between the working duration and the diameter of right main bronchus ($r = -0.366$, $p = 0.020$). A positive correlation was seen between smoking and the right upper bronchus wall thickness ($r = 0.457$, $p = 0.005$)." Findings were not reproducible across anatomic airways sites
Suyur et al (2012) ⁵⁷	Observational, with control (cross-sectional)	Workers ($n = 104$) at 2 PVC production plants and 43 administrative controls evaluated by HRCT. HRCT revealed pleural and/or parenchymal changes in 55% of the exposed subjects. Pleural thickening was detected in 14 subjects, 13 of whom were in the exposed group ($p < 0.05$). Isolated pleural thickening without parenchymal involvement was present in 7 workers, who were all in the exposed group ($p < 0.05$). Pleural thickening was frequently bilateral and localized to the parietal and visceral pleura. Round opacities, heterogeneous attenuation, and ground-glass opacities were only detected in the exposed group ($p < 0.05$). Exposure to dust increased the risk of findings on HRCT (OR 4.2, $p < 0.05$). It was concluded that exposure to PVC dust, at levels below the legal limit for respirable particulate matter, was associated with parenchymal changes and pleural thickening on HRCT
Thrumurthy et al (2010) ⁷	Observational, no control (case report)	Case report describing a coal miner who presented with HRCT findings of diffuse interlobular septal thickening. Usual causes other than coal mine dust exposure were ruled out. He died with severe secondary pulmonary hypertension. A postmortem examination revealed lung fibrosis with areas of anthracotic pigment, anthracotic nodules, as well as changes of pulmonary hypertension and right ventricular hypertrophy.

Subject area/reference	Type of study	Comment
Tiwari (2013) ⁷⁵	Observational, no control (cross-sectional)	Evaluated "22 workers exposed to fibrogenic dust by virtue of their occupation in a factory." All but one at least 40 y old. Evaluated by CXR by 3 readers; do not appear to have used ILO system. One reader evaluated HRCT. Six found to have "interstitial lung fibrosis" by HRCT; 4 of these had a normal CXR. One each had combined interstitial lung fibrosis and TB by HRCT and CXR. Authors found poor agreement between HRCT and CXR, with a kappa value of 0.34
Tutkun et al (2014) ⁵³	Observational, no control (cross-sectional)	Male welders ($n = 74$, mean age 41 y) mean duration of exposure = 19 y evaluated by CXR and HRCT. Two radiologists evaluated each. Structured evaluation methods were not noted in methods. "Although all were found to be nonpathological on the CXR, 27 mild nodular, and 9 mild linear opacities, 5 emphysematous changes, 3 ground-glass infiltrates, and 1 pleural thickening were detected by HRCT." Concluded that "HRCT provides better diagnostic performance compared to CXR for the diagnosis of welder lung disease"
FDG-PET/CT^c		
Niccoli-Asabella et al (2013) ⁵⁸	Observational, no control (case series)	Retrospective evaluation of FDG-PET/CT in evaluating 57 patients with epithelial malignant mesothelioma. In the authors' experience, it has greater sensitivity than CT with contrast enhancement in identifying local extent, lymph nodes, and metastasis
Yu et al (2013) ⁵⁹	Observational, no control (case series)	Authors report 4 cases (asbestos textile worker with asbestosis, quarry worker with silicosis, quarry worker with history of silicotuberculosis, tunnel worker with silicosis) where FDG-PET/CT was able to differentiate between cancer and pneumoconiosis and was useful in patient management. Authors note previous literature of increased FDG uptake in pneumoconiosis and disagreement in literature about usefulness of PET scanning in the presence of pneumoconiosis. Feel that their experience suggests usefulness
Coronary/thoracic artery calcification		
Lee et al (2013) ⁷⁶	Observational, no control (cross-sectional)	Subjects ($n = 76$) "exposed to inorganic dusts" underwent chest CT scanning with a multidetector CT scanner. They were evaluated for coronary artery calcification and pneumoconiosis. They also underwent pulmonary function testing. FEV ₁ /FVC (%) fell and total calcification scores significantly increased significantly with age. Total calcification scores were significantly negatively correlated with FEV ₁ /FVC (%). The frequency of the subjects with pneumoconiosis in the calcified group (63%) was higher than that in the noncalcified group (44%)
Vehmas (2012) ²⁴	Observational, no control (cohort)	Evaluated 504 men, mean age 63 y, who had undergone spiral CT for lung cancer screening for visual chest atherosclerotic calcifications and assessed for relationship to mortality after a mean follow-up time of 10 y. Calcifications in the aortic arch (HR: 1.35) and brachiocephalic origin (HR: 1.45) were independent predictors of all-cause deaths. Calcifications in the left anterior descending artery (HR 1.86) and brachiocephalic calcifications (HR 1.65) were independent predictors of cardiovascular death
Yankelevitz et al (2013) ⁶⁰	Observational, no control (cohort)	Evaluated a cohort of 3,048 never smokers participating in lung cancer screening through the Flight Attendant Medical Research Institute International Early Lung Cancer Action Program. They had low-dose chest CT scans. The presence and extent of coronary artery calcification was associated with the extent of second-hand tobacco smoke exposure, even after adjusting for other risk factors for coronary artery calcification. Adjusted OR were 1.54 for low exposure, 1.60 for moderate exposure, and 1.93 for high exposure

Abbreviations: BMI, body mass index; CI, confidence interval; CT, computed tomography; CXR, chest X-ray; DLCO, diffusing capacity of the lung for carbon monoxide; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; HR, hazard ratio; HRCT, high-resolution CT; ICOERD, International Classification of HRCT for Occupational and Environmental Diseases; ILD, interstitial lung disease; ILO, International Labor Organization; LDCT, low-dose CT; NLST, National Lung Screening Trial; OR, odds ratio; PMF, progressive massive fibrosis; PVC, polyvinyl chloride; TB, tuberculosis; TLC, total lung capacity; WTC, World Trade Centre.

^a International Classification of HRCT for Occupational and Environmental Respiratory Diseases.

^b International Labor Organization.

^c 18-fluorine-labeled 2-deoxy-2-fluoro-D-glucose positron emission tomography/computed tomography.

Table 2

Reviews identified by literature search

Subject area/reference	Systematic review (Y/N)	Comment
CT in ORD—General		
Cox et al (2014) ⁷⁷	No	Shows spectrum of HRCT imaging patterns in ORD
Farzaneh et al (2010) ⁷⁸	No	General review of imaging aspects of inhalational lung diseases
Flors et al (2010) ⁷⁹	No	Describes CT findings in siderosis, talcosis, berylliosis, calcicosis, hypersensitivity pneumonitis (due to wheat flour and isocyanates), and Ardystil syndrome
Furlow (2011) ⁸⁰	No	General review of occupational lung diseases
Larici et al (2014) ⁸¹	No	General review of imaging in occupational and environmental lung disease
Pipavath et al (2010) ⁸²	No	General review of imaging in occupational and environmental lung disease, including HCRT patterns
Satija et al (2013) ⁸³	No	General review of imaging in ORD
Sirajuddin and Kanne (2009) ⁸⁴	No	General review of imaging in ORD
CT in ORD—Specific diseases		
Kreiss (2013) ⁶¹	No	Notes CT findings in OB
Lynch et al (2012) ⁶³	No	Notes CT findings in OB
Machiori et al (2010) ⁸⁵	No	Reviews CT findings in pulmonary talcosis
Sharma et al (2010) ⁸⁶	No	Reviews CT features of chronic beryllium disease
Wilken et al (2011) ⁹	Yes	Systematic review and meta-analysis of lung function in asbestos-exposed workers, including lung function changes associated with radiographic findings. Meta-analysis with data from 9,921 asbestos-exposed workers found statistically significant reduction in VC, FEV ₁ and FEV ₁ /VC that was related to extent of radiographic findings. Less severe lung function impairments were detected if the diagnoses were based on HRCT instead of plain chest images
CT in ILD		
Alhamad and Cosgrove (2011) ⁸⁷	No	Reviews clinical approach to ILD, including HRCT findings
Gulati (2011) ⁸⁸	No	Reviews clinical approach to ILD, including HRCT findings
Jawad et al (2012) ⁸⁹	No	Reviews use of HRCT in ILD
Poletti et al (2012) ⁹⁰	No	Focuses on idiopathic nonspecific interstitial pneumonia; notes that pattern can occur after occupational exposure
CT screening for lung cancer		
Ollier et al ^a (2014) ¹¹	Yes	Systematic review and meta-analysis of cohort studies involving screening of asbestos-exposed workers
Vehmas et al ^a (2014) ¹⁰	Yes	Systematic reviews of low-dose CT screening for lung cancer and screening asbestos-exposed workers
No authors listed (2011) ⁹¹	No	Report from the American Statistical Association's 2010 conference on radiation exposures in medicine

Abbreviations: CT, computed tomography; HRCT, high-resolution CT; ILD, interstitial lung disease; OB, obliterative bronchiolitis; ORD, occupational respiratory disease; VC, vital capacity.

^aNot recovered by PubMed search described in methods.